MRI Diagnosis of Brainstem Cavernous Angiomas Presenting as Tumours
Mark C. Preul, Jean-Guy Villemure, Richard Leblanc and Raquel del Carpio-O’Donovan

ABSTRACT: We report experience with 11 patients misdiagnosed for years, on the basis of computed tomography (CT) and angiography, as harbouring brainstem tumours in whom magnetic resonance imaging (MRI) demonstrated cavernous angiomas. Seven had undergone external irradiation, 2 had a ventriculo-peritoneal shunt, 2 developed aseptic femur necrosis following corticosteroid treatment, 1 had undergone a biopsy with a pathological diagnosis of glioma. CT had depicted ill-defined, hyperdense, faintly enhancing lesions. Angiography was normal, or showed an avascular mass or subtle venous pooling. MRI delineated discrete lesions, typical of cavernous angiomas, with a mixed hyperintense, reticulated, central core surrounded by a hypointense rim. Six patients subsequently underwent stereotactic radiosurgery without changes in clinical status or lesion. Although hemorrhagic neoplasms may mimic the clinical course and MRI appearance of cavernous angiomas, MRI is useful in the diagnosis of brainstem cavernous angiomas and should be performed in patients with suspected brainstem tumours.

RÉSUMÉ: Diagnostic par MRI des angiomes caverneux du tronc cérébral se présentant comme des tumeurs. Nous rapportons les cas de 11 patients diagnostiqués à tort pendant des années, sur la base de la tomodensitométrie (CT) et de l’angiographie, comme étant porteurs de tumeurs du tronc cérébral, chez qui l’imagerie par résonance magnétique (MRI) a démontré des angiomes caverneux. Sept avaient subi une irradiation externe, 2 avaient subi un shunt ventriculo-péritonéal, 2 avaient développé une nécrose aseptique du fémur suite au traitement par des corticostéroïdes et 1 avait subi une biopsie dont le diagnostic anatomopathologique était celui de gliome. Le CT avait montré des lésions mal définies, hyperdenses, faiblement rehaussées par la substance de contraste. L’angiographie était normale ou montrait une masse avasculaire ou une accumulation veineuse discrète. La MRI a défini des lésions discrètes, typiques d’angiomes caverneux, avec un noyau central hyperintense, réticulé, entouré d’une bordure hypo-intense. Six patients ont subi une radiochirurgie stéréotaxique par la suite, sans changement dans le statut clinique et sans lésion. Bien que les néoplasies hémorragiques puissent imiter l’évolution clinique et l’aspect des angiomes caverneux à la MRI, cette dernière est utile au diagnostic des angiomes caverneux et devrait être pratiquée chez les patients chez qui on suspecte des tumeurs du tronc cérébral.


Brainstem cavernous angiomas can mimic pontine hemorrhages, demyelinating disease, or neoplasms.1-13 The differentiation of cavernous angiomas from pontine hemorrhage and demyelinating disease is well described, but few reports address the tumour-like presentation of cavernous angiomas. As cavernous angiomas and brainstem tumours are treated differently, it is important to differentiate the two. This can readily be achieved with magnetic resonance imaging (MRI). A series of patients with cavernous angiomas initially misdiagnosed and treated for years as having brainstem neoplasms has not previously been reported.

We described a group of 11 such patients found to harbour a probable brainstem cavernous angioma based on the MRI appearance of their lesions and discuss the treatment of patients with cavernous angiomas who were previously treated for brainstem neoplasms.

PATIENTS AND METHODS

Eleven patients with a brainstem cavernous angioma initially misdiagnosed as glioma (9 cases), glioma or pinealoma (1 case), and glioma, other third ventricle tumour or aneurysm (1 case) were seen over a 38 month period (Table 1). They comprise a subset of over 40 patients with a brainstem cavernous angioma referred to our institution over the past 5 years. All patients had a fluctuating clinical course over the 1 to 23 years following initial diagnosis of brainstem tumour and were referred to our institution after acute exacerbation of symptoms. One patient had undergone a posterior fossa craniectomy and biopsy of his lesion which was interpreted as a low grade glioma at pathological examination. They had previously been treated with whole brain irradiation (7 cases), ventricular shunting (2 cases), and long term corticosteroids (8 cases). The latter treatment had pro-
duced bilateral femoral aseptic necrosis in 2 cases. Follow-up ranged from 18 to 42 months (mean 30 months).

Non-contrast computed tomography (CT) depicted an ill-defined, hyperdense lesion in all cases. Faint contrast enhancement was identified in 8 of 10 cases and 1 showed marked enhancement (one patient did not have a contrast-infused CT). The cavernous angioma of one patient showed no contrast enhancement (one patient did not have a contrast-infused CT). Follow-up enhancement on one CT scan, although 6 months later, there was marked enhancement. Angiography (including delayed venous phase and subtraction imaging) showed a mass lesion with adjacent vessel displacement in 3 patients; and venous pooling in another. Three patients had a normal angiogram (Table 2).

Magnetic resonance imaging was performed with a 1.5 Tesla scanner (Phillips Gyroscan, The Netherlands) using T1-weighted (TR = 550 ms, TE = 30 ms), proton density and T2-weighted (TR = 2000-2100 ms, TE = 30, 60-80 ms) spin echo pulse sequences with two excitations. Multiple slice data acquisition was used, acquiring 6-8 mm thick slices with a 256 x 256 matrix. The lesions were delineated distinctly in all cases. The volume of the lesions ranged from 2.6 cm³ to 35 cm³. The lesions and clinical progression of 10 of 11 patients were studied with serial MRI scans.

The diagnosis of cavernous angioma was made on the basis of the demonstration of a characteristic, heterogeneous (mainly hyperintense), reticulated, central core surrounded by a prominent hypointense rim, with absence of edema, and of feeding or draining vessels on T2-weighted and proton density images.14-18 The cavernous angiomas were localized to the pons and extended to the pontomedullary junction, the posterior third ventricle (thalamus), to the cerebellum, and the cerebral peduncles (Table 2).

Six patients were treated by stereotactically focussed radiosurgery.19 The size of their lesions ranged from 2.6 to 20 cm³ and they received 3500 to 4500 cGy to the cone (1.0 to 2.0 cm diameter), and 1750 to 2250 cGy (50% isodose line) to the periphery of the lesions. There was no clinical improvement or deterioration with this treatment, and the lesions did not change in size as a result of it, as seen on sequential MRI studies. Two patients with associated hydrocephalus were treated with a ventriculo-peritoneal shunt and improved clinically. Clinical follow-up, with MRI, of the patients after receiving stereotactic radiosurgery ranged from 20 to 42 months (mean 34 months) (Table 3).

ILLUSTRATIVE CASES AND MRI CORRELATION

Patient 1
J.A. (male, age 36 years) was hospitalized in 1977 for acute onset of diplopia, unsteadiness, dysarthria, and decreased sensation of the left face. Neurological examination showed an alert patient with slow dysarthric speech, a left sixth nerve paresis, nystagmus on vertical and left gaze, jerky saccades in all directions, hypesthesia over the left face, left side hypertonia and hyperreflexia with a left Babinski sign, dysdiadochokinesia and ataxia of all extremities (right arm more than left), and gait and truncal ataxia. Skull radiograms showed posterior displacement of the pineal gland suggesting an enlarged brainstem. Pneumoencephalography demonstrated an intrinsic mass lesion in the pons, mesencephalon, and the medulla. Computed tomography showed a mildly hyperdense, mildly enhancing lesion in the right pons and (Figure 1 - A, B and C) an angiogram showed an avascular mass in the pons and mesencephalon. A pontine glioma was diagnosed and he was treated with external beam radiotherapy (5600 cGy) and corticosteroids. He improved and was discharged home, able to walk independently. He remained well with very mild fluctuating symptoms until 1988 when he had headache and significant exacerbation of previous neurological symptoms. J.A. was treated by stereotactically focussed radiosurgery and they received 3500 to 4500 cGy to the cone (1.0 to 2.0 cm diameter), and 1750 to 2250 cGy (50% isodose line) to the periphery of the lesions. There was no clinical improvement or deterioration with this treatment, and the lesions did not change in size as a result of it, as seen on sequential MRI studies. Two patients with associated hydrocephalus were treated with a ventriculo-peritoneal shunt and improved clinically. Clinical follow-up, with MRI, of the patients after receiving stereotactic radiosurgery ranged from 20 to 42 months (mean 34 months) (Table 3).

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<tr>
<th>Table 2: Imaging Characteristics</th>
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<td><strong>Modality</strong></td>
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<td>low density lesion</td>
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<td>enhancement</td>
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<td>calcium</td>
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<td>recent hemorrhage</td>
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<td>Angiography (n = 7)</td>
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<td>normal</td>
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<td>avascular mass</td>
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<tr>
<td>venous lake</td>
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<td>MRI (n = 11)</td>
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<tr>
<td>reticulated, heterogeneous signal surrounded by prominent hypointense rim (T2 and proton density)</td>
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<tr>
<td>hemorrhage: active</td>
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<td>methemoglobin</td>
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<td>hemosiderin</td>
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<td>size (cm³): 2.6-35 (range)</td>
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<td>Lesion location and extension based on MRI (N = 11)</td>
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<tr>
<td>pons</td>
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<td>cerebellar peduncle</td>
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Patient 2

orbital headache and felt ill for several days with right-sided hearing loss, dysarthria, decreased hearing, diplopia, and right spastic hemiplegia. Computed tomography showed that the mass was larger and a diagnosis of malignant glioma was formulated. She was treated with corticosteroids and radiotherapy (5600 cGy). She improved over four months, but she again developed severe headache, dysarthria, decreased hearing, diplopia, and right spastic hemiplegia. Angiography was normal. A diagnosis of brainstem tumour was made and he was treated with corticosteroids. He was referred to our care in 1987. Examination at that time showed horizontal nystagmus on lateral gaze to each side, right face hypesthesia with decreased corneal reflex, uvula deviated to the right, complete right-sided hypesthesia, slight dysdiadochokinesia with mild hemiparesis on the right. Non-contrast CT revealed a large, slightly hyperdense, ill-defined lesion in the inferior left thalamus, midbrain, and pons (Figure 3 - A and B). Magnetic resonance imaging disclosed a cavernous angioma (volume 20 cm³) in the mid and left pons involving both cerebellar peduncles, and extending to the left inferior thalamus (Figure 3 - C and D). He underwent stereotactic radiosurgery (4500 cGy, 2.0 cm cone). His clinical state and the appearance of his lesion are unchanged.

Patient 3

P.B. (male, age 23 years) developed sudden onset of right-sided paralysis and dysarthria. The right-sided paralysis resolved spontaneously over two months, although he remained dysarthric. Eight years later, he developed right hemiparesis over a period of two weeks that did not resolve. Neither event was associated with headache. In 1986, he had gradual worsening of his hemiparesis and the onset of a bilateral intention tremor worse on the right side, again without headache. Computed tomography identified a hyperdense mass in his brainstem. Angiography was normal. A diagnosis of brainstem tumour was made and he was treated with corticosteroids. He was referred to our care in 1987. Examination at that time showed horizontal nystagmus on lateral gaze to each side, right face hypesthesia with decreased corneal reflex, uvula deviated to the right, complete right-sided hypesthesia, slight dysdiadochokinesia with mild hemiparesis on the right. Non-contrast CT revealed a large, slightly hyperdense, ill-defined lesion in the inferior left thalamus, midbrain, and pons (Figure 3 - A and B). Magnetic resonance imaging disclosed a cavernous angioma (volume 20 cm³) in the mid and left pons involving both cerebellar peduncles, and extending to the left inferior thalamus (Figure 3 - C and D). He underwent stereotactic radiosurgery (4500 cGy, 2.0 cm cone). His clinical state and the appearance of his lesion are unchanged.

Patient 3 differs from patients 1 and 2 in that, although he had a very large lesion, his course was not characterized by stepwise deteriorations, but instead he had more progressive decline leading to moderate disability. There was no evidence of hemorrhage on CT or MRI for this patient. His clinical deterioration was most likely due to the slow, but progressive expansion of the cavernous angioma.

MRI Correlation

The appearance of the cavernous angioma on MRI correlated with the clinical state of the patient. Patients with mild neurological deficit had cavernous angiomas with a mean volume of 4.0 cm³; those with a moderate neurological deficit had a cavernous angioma with a mean volume of 8.7 cm³; and patients with a severe neurological deficit had lesions with a mean volume of 21 cm³. Four patients had evidence of recent significant hemorrhage on CT or MRI. None of these patients had hemorrhage on CT or MRI for this patient. His clinical deterioration was most likely due to the slow, but progressive expansion of the cavernous angioma.

DISCUSSION

Angiographically occult vascular malformations

Margolis, et al., and Potter, first drew attention to the importance of small, angiographically occult vascular anomalies as a cause of cerebral hemorrhage. Crawford and Russell introduced the term "cryptic" to describe these lesions 22-25 and Krayenbuhl stressed that hemorrhage from cryptic malformations could be due to cavernous angiomas. With the advent of CT and MRI, angiographically occult cerebral vascular malformations have been recognized with increasing frequency and the characteristic appearance of cavernous angiomas has been described. 12,14,15,17,18,28-31 The tendency to diagnose and treat brainstem angiographically occult vascular malformations such as cavernous angiomas has paralleled the introduction, spread, and refinement of MRI. 32-36
Presentation of brainstem cavernous angiomas

Brainstem cavernous angiomas may present acutely with a catastrophic brainstem hemorrhage, or exhibit a more chronic, progressive course due to increased size and repeated microhemorrhages. The clinical diagnosis of brainstem cavernous angiomas can be difficult: of 138 patients with pathologically verified cavernous angiomas studied by Simard et al., 10 of 49 presenting with signs and symptoms consistent with a mass lesion involved the brainstem. The noncatastrophic neurological deterioration of patients with brainstem cavernous angiomas is thought to result from slow, progressive ectasia of vascular sinusoids. Recurrent microhemorrhages with resultant occlusion of vascular channels and subsequent organization, fibrosis, and calcification may also contribute to the progressive deterioration. Internal hemorrhages located between contiguous sinusoids also may create cysts.

The most common course of our patients was progressive deterioration marked by sudden episodes of neurological decompensation that suggested the initial diagnosis of brainstem glioma. Four of our 11 patients presented with a brainstem hemorrhage and CT and MRI of the patient admitted in coma showed the largest hemorrhage. The hemorrhage as noted on CT and MRI was coincident with recent clinical deterioration. Furthermore, upon review of previous outside CT and pneumoencephalographic studies, it was noted that the size of the lesion or mass effect correlated with the coincident clinical deterioration at that particular time. Cavernous angiomas in our cases had produced significant morbidity: 8 of our patients had onset of symptoms at 23 to 36 years, and 8 were moderately or severely disabled at admission to our institution. The size (volume) of the angioma and evidence of recent hemorrhage within the lesion on MRI at our institution correlated with the clinical presentation.

Differentiating brainstem cavernous angiomas and gliomas

Cavernous angiomas are usually isodense or slightly hyperdense on CT, may display punctate calcification, and enhance weakly with the intravenous infusion of contrast material. Furthermore, as seen in one of our patients, the degree of enhancement of the same cavernous angioma following contrast
Figure 2 — Patient 2 C.K. Non-contrast CT (A) displays slightly hyperdense, ill-defined mass in the pons, left midbrain, extending to the left thalamus. Contrast-infused CT (B) shows minimal enhancement. MRI T2 (TR 2000 TE 60) sagittal (C) and T2 (TR 2100 TE 60) axial (D) display a 35 cm³ cavernous angioma situated in the pons, left cerebellar peduncle, mesencephalon, reaching to the medial and posterior portions of the left thalamus. There is a 1 cm³ area of high signal intensity consistent with methemoglobin in the mesencephalon and thalamus that represents recent hemorrhage which correlated with her most recent clinical deterioration.

material infusion may vary from little or no enhancement to marked enhancement on CT scans over a period of time. Gliomas of the brainstem are commonly isodense or hypodense, and do not usually enhance with contrast. Interpretation of a minimally enhancing isodense or hyperdense, ill-defined lesion in the brainstem on CT is difficult as these findings are consistent with a diagnosis of low grade astrocytoma, oligodendroglioma, granuloma, or cavernous angioma. Magnetic resonance imaging can identify the characteristic signal alteration of old hematomas, and is more specific than CT to diagnose cavernous angiomas. However, Sze, et al., have stressed the difficulty of differentiating angiographically occult vascular malformations from hemorrhagic neoplasms on MRI. The presence of edema may allow the difference to be made, although, a degree of edema also may be seen around angiographically occult vascular malformations that have recently bled. Significant hemorrhage occurs in only 1-3% of primary brainstem gliomas, and produces significant morbidity and mortality. Hemorrhage in a brainstem cavernous angioma is often well tolerated, perhaps because they are smaller and their tenuous sinusoidal and cystic components act as buffers to absorb some of the sudden shock of hemorrhage. Cavernous angiomas retain a characteristic methemoglobin signal on MRI; whereas, resolution and clearing of methemoglobin, leaving a hemosiderined, fluid-filled cavity, is expected with hemorrhage within a tumour. Sequential MRI should reveal progression of neoplasms or the regression of the edema associated with cavernous angiomas as the hematoma resolves. The term cavernous angioma, instead of occult vascular malformation, is used in this paper with the knowledge that although a characteristic MRI appearance has been described for cavernous angiomas, it may, in fact, not be able to distinguish cavernous angiomas from capillary telangiectasias, or small, thrombosed venous angiomas and arteriovenous malformations in all cases.

Treatment

All eleven patients were felt to have inoperable cavernous angiomas because of size and/or location. Thus, 6 patients underwent stereotactically focussed irradiation via a linear accelerator. There was no change in lesion size or in the patients’ clinical condition at the time of last follow-up using sequential
MRI studies for comparison. However, recent studies, which included these 6 patients, on the efficacy of stereotactic radiosurgery for occult cerebral vascular malformations such as cavernous angiomas suggest that unlike arteriovenous malformations, stereotactic radiosurgery by gamma knife or linear accelerator does not appear to obliterate cavernous angiomas.19

Those patients whose lesion is relatively small and in a location in the brainstem that is easily accessible (such as in the fourth ventricle, subependymal, or with minimal intervening neural tissue), that have produced repeated hemorrhages or recent life-threatening hemorrhage, should be considered for surgery. Patients such as ours with very large angiomas or with angiomas in an inaccessible location should be offered palliative therapy such as CSF shunting when indicated.

Still to be defined is the rationale for treating those patients with an incidental brainstem cavernous angioma or with an angioma in a difficult location that has bled only once. Only further longitudinal studies comparing the natural history of cavernous angiomas to the risks of surgery will provide guidance to the surgeon.

We conclude that MRI is superior to CT and angiography in diagnosing brainstem cavernous angiomas, and that MRI should be performed in patients with a presumptive diagnosis of brainstem tumour on the basis of CT and angiogram.

REFERENCES


